## REMARKS

The informalities in Claim 1 have been corrected. Claim1 has been amended to specify oral administration of cystine or cysteine.

Support for this is found at page 4 line 2 of the specification.

Applicant's attorney is advised that the only relevant copending application of the applicant is WO 01/02004. Prior application 09/926,363 has been abandoned and has no surviving progeny.

WO 01/02004 is referred to in the present application but discloses a different compound, N-acetyl cysteine for intravenous administration for treatment of oxidative stress in hemodialysis. Applicant's attorney is advised that N-acetyl cysteine is currently available I the United States as an intravenous antidote to paracetamol (acetaminophen) intoxication.

Having regard to the "test note" referred to in the previous response, what happened to it is unclear. However, the applicant now sets out the contents thereof as a declaration and this is enclosed.

On the question of the written description requirement, claim 1 has been amended to replace the word "preventing" by the word "inhibiting". The examiner accepts that there is adequate description of treatment but questions whether what is described could effect total prevention. The issue here is one of language. Although the applicant does not necessarily agree with this interpretation, the word "treatment" could be construed as requiring that a condition has been diagnosed before there would be infringement of it. If such a meaning is given, a claim confined to "treatment" would not be construed to cover a prophylactic use, even though the same biochemistry is involved. The recitation of the alternative of "inhibition" in amended Claim 1 is

intended to cover such a situation. It is submitted that there is adequate written description to support such a claim term and to show that the applicant had possession of the invention so-defined at the time of filing the application.

Turning now to rejection under 35 USC 103(a), the examiner adds Sela et al., to the art cited previously. The teachings of this reference, however, really add little to what is acknowledged in te application, namely that patients undergoing hemodialysis have been observed to be subject to oxidative stress. It teaches the use of heparin, a commonly used anticoagulant to treat this. Such teaching does not, however, point to the use of cystine or cysteine for such a purpose.

Nor does it suggest any oral composition for treating or inhibiting oxidative stress. Heparin is injected or dripped into the patient.

As noted in response to the previous action, Yamamoto describes the use of cysteine to treat diabetic complications. It contemplates effecting this by a daily dose of from 10 - 5000 mg ( see column 3 lines 3 - 4 and column 4 lines 29 - 34.. That is to say by continuous treatment with cysteine to effect a long term chronic complications of diabetes, not a specific dose administrations at specific times associated with a particular event, namely hemodialysis at a particular time to treat an acute condition brought about by that treatment. Furthermore, as noted previously, but not commented on by the examiner, Yamamoto talks generally about use of cysteine to treat diabetic complications, but the only definite information given is with respect to cataracts and that in rats treated with cysteine, serum chemical parameters were close to normal in male SD rats in which diabetes had been induced by streptozotocin injection. As pointed out previously streptozotocin induces diabetes by destruction of pancreatic cells thereby preventing insulin production. This is therefore an insulin-dependent form of diabetes (Type 1). The types of condition referred to in the present claims are typically those resulting from non-insulin dependent diabetes.(Type 2) Insulin dependent diabetes is normally treated by insulin injections rather than by

hemodialysis.

Dall'Aglio teaches that a combination of tioctic acid and cysteine may be used to treat conditions caused by oxidative stresses and alterations of mitochondrial energetic metabolism. Diabetes (of no particular type) is mentioned as one of a large number of possible causes of oxidative stress.

Indeed pages 3 - 5 of Dall'Aglo list such a wide variety of conditions that it says can be improved by use of a drug, cosmetic or dietetic supplement that utilizes the synergistic effect of a combination of these two compounds or their derivatives that it almost seems that the authors are describing the universal panacea. However, none of these seems related to diabetes or kidney disease. Certainly no experimental data are reported that are directly relevant to kidney failure. The experimental data do, however, point to the need to use a combination of cysteine and tioctic acid to achieve the desired relief of oxidative stress. importance of both components being set out, for example in the conclusions set out on page 31.

This does not therefore teach the use of cysteine alone to treat oxidative stress.

The art therefore teaches that cysteine can be used to treat diabetes by long term administration of regular doses of cysteine. It also teaches that kidney disease may be caused by diabetes. However, neither fact is really irrelevant to the present invention which relates to specific doses in conjunction with specific treatments that do not take place daily. (Hemodialysis is typically carried out a few times per week, but not daily) . The art teaches that a combination of cysteine and tioctic acid may be useful in treating various types of oxidative stress, none of which seems directly related to kidney disease or hemodialysis. But it does not teach any such utility for cysteine alone. Although it is known that hemodialysyis may cause oxidative stress, it does not follow from what is described in the art that cysteine is itself an effective way to combat that oxidative stress. The art does not teach or in anyway suggest that specific problems that arise when patients are

subject to hemodialysysis may be treated or inhibited by use of cysteine.. The present claims are limited to this and are therefore novel and non-obvious over this art. In particular claim 10 is specifically directed to a method in which the relationship of the treatment with cysteine or cystine with the dialysis is specifically set out. Nothing in the art points to administering a single dose of cysteine before or after hemodialysis to combat the oxidative stress caused by that dialysis.

It is therefore submitted that the requirements of 35 USC 103 have been complied with and that this application should be allowed.

Respectfully submitted,

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